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{Review Article}

Rutin: A Multifunctional Flavonoid with Broad-Spectrum Therapeutic Potential

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Abstract

Rutin (quercetin-3-O-rutinoside) is a widely distributed flavonol glycoside that has attracted sustained interest as a multifunctional phytochemical with antioxidant, anti-inflammatory, cardioprotective, neuroprotective, anticancer, metabolic, and organ-protective effects. Contemporary phytochemistry has clarified its structural features, major botanical sources (notably *Sophora japonica* and buckwheat), and advances in green extraction and analytical technologies that enable reliable standardization of rutin-rich extracts. At the same time, pre-clinical and early clinical data have expanded understanding of its pharmacodynamic actions, including modulation of redox homeostasis, inhibition of NF-κB–driven inflammation, improvement of endothelial function, regulation of lipid and glucose metabolism, and targeting of multiple oncogenic signaling pathways. Large-scale reviews and emerging mechanistic work also highlight longstanding challenges: low aqueous solubility, modest oral bioavailability, and variability in content across plant matrices.

This review synthesizes recent evidence on rutin with particular emphasis on its phytochemical profile and pharmacological activities spanning antioxidant, cardiometabolic, neuroprotective, anticancer, hepatoprotective, nephroprotective, antimicrobial, and antiviral domains. Special attention is given to clinically relevant data, such as a randomized controlled trial where oral rutin improved blood pressure and antioxidant status in patients with type 2 diabetes mellitus and to nano- and formulation-based strategies designed to overcome biopharmaceutical limitations. Finally, we outline key research gaps, including the need for well-designed dose-finding clinical trials, standardized nutraceutical preparations, and integration of computational approaches to guide rational drug design.

Keywords: *Rutin; quercetin-3-O-rutinoside; flavonoid; antioxidant; cardioprotection; neuroprotection; hepatoprotection; nephroprotection; antimicrobial; antiviral.*

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1. Introduction

Flavonoids are polyphenolic secondary metabolites abundantly present in fruits, vegetables, herbs, and beverages such as tea and wine. They are broadly grouped into flavonol, flavones, flavanones, flavan-3-ols, anthocyanidins, and isoflavones, and contribute to plant defense, pigmentation, and human nutrition [1,2]. Among these, rutin, chemically quercetin-3-O-rutinoside, is one of the most extensively studied flavonol [1–3]. It occurs in numerous edible and medicinal plants and has attracted attention as a nutraceutical candidate because of its pleiotropic pharmacological activities and generally favorable safety profile [1–4].

Over the last decades, phytochemical and pharmacological studies have re-positioned rutin from a classical "vitamin P" type vasoprotective bioflavonoid to a multitarget agent with cardiovascular, neuroprotective, anticancer, and organ-protective potential [1–4]. Rutin and its aglycone quercetin exert strong antioxidant and anti-inflammatory effects and modulate multiple signaling pathways, including NF-κB, Nrf2/ARE, MAPK, PI3K/Akt, SIRT1, and apoptotic cascade [1–4]. These properties underpin a wide range of experimentally demonstrated benefits in cardiometabolic, neurodegenerative, hepatic, renal, and oncologic models.

From a natural products perspective, rutin is attractive because it is highly enriched in accessible plant sources such as buckwheat (*Fagopyrum esculentum*), *Sophora japonica* flower buds, and several fruits and vegetables [3,5–8]. Functional food and nutraceutical formulations derived from these sources provide a pragmatic route to translate experimental findings into human use. At the same time, recent work emphasizes unresolved challenges: low aqueous solubility, modest oral bioavailability, extensive first-pass metabolism, and variability in content across plant matrices [3,4].

2. Phytochemical Profile of Rutin

2.1 Chemical Structure and Classification

Rutin is a flavonol glycoside consisting of the aglycone quercetin linked via an O-glycosidic bond at the 3-position to the disaccharide rutinose (α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranose) (Fig. 1) [1–3,9]. Its molecular formula is $C_{27}H_{30}O_{16}$ and its molecular weight is approximately 610.5 Da.[9] The core flavonol scaffold confers conjugated double bonds and multiple hydroxyl groups, particularly in the B-ring (3′,4′-dihydroxy), which are critical for radical scavenging and metal chelation [1,2].

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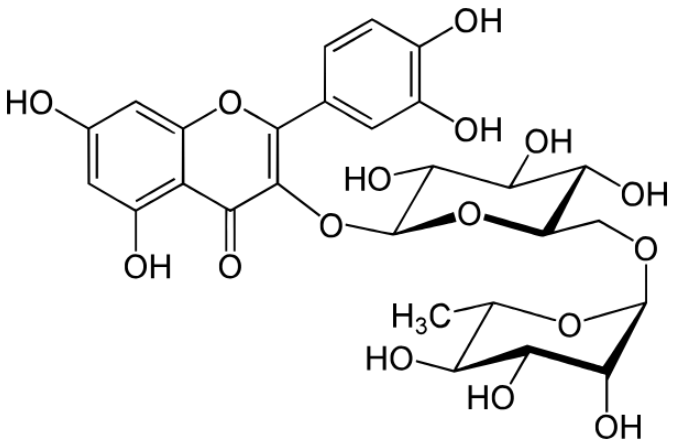

Fig. 1: Structure of Rutin

Structurally, rutin belongs to the class of flavonoid-3-O-glycosides, which show distinct physicochemical and pharmacokinetic properties compared with their aglycones [3,4]. Glycosylation at C-3 increases hydrophilicity, improves stability in the gastrointestinal lumen, and modulates absorption mechanisms (via active transporters and microbiota-mediated deglycosylation), but it may reduce passive membrane permeability and oral bioavailability [3,4]. Rutin is often regarded as a "pro-phytochemical" reservoir for quercetin because enzymatic or microbial deglycosylation can regenerate the aglycone in vivo, while the intact glycoside itself exhibits specific cell-type and tissue-specific activities [3,4].

2.2 Natural Sources and Extraction

2.2.1 Plant sources

Rutin is widely distributed in the alimentary and medicinal plants. Buckwheat is one of the richest dietary sources: buckwheat leaves and flowers may contain several grams of rutin per kilogram of dry weight, and rutin remains present in flours and groats used for human consumption [5,6,10]. *Sophora japonica* (Japanese pagoda tree) represents an important industrial source; the flower buds and young leaves can accumulate high levels of rutin and related flavanols and are commonly used for commercial extraction [7,8]. Citrus peels (especially orange and lemon), as well as their leaves, also contain substantial levels of rutin and other flavanones and flavanols [11].

Beyond these, rutin has been identified in apples, onions, grapes, elderberry (*Sambucus nigra*), *Morus alba*, *Dimorphandra* species, and numerous medicinal herbs used in traditional systems of medicine [3,7,11]. The abundance of rutin in commonly consumed foods makes dietary enrichment feasible and underpins many of the epidemiological associations between polyphenol-rich diets and reduced cardiometabolic risk [2,3,6].

2.2.2 Conventional extraction

Conventional extraction of rutin from plant materials typically employs aqueous-alcoholic solvents (ethanol, methanol, hydroethanol) using maceration, reflux, or Soxhlet techniques

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[3]. Rutin is moderately soluble in ethanol and methanol but poorly soluble in water, necessitating organic or mixed solvents [3]. Early work on *S. japonica* demonstrated that methanolic extraction affords high rutin recovery and that ultrasound-assisted extraction can significantly reduce extraction time while increasing yield, although purely aqueous ultrasonication may generate radicals that degrade the compound [13].

2.2.3 Green and advanced extraction

Driven by environmental and regulatory pressures, deep eutectic solvents (DES) and natural deep eutectic solvents (NADES) have emerged as "green" alternatives to conventional organic solvents [3,14–16]. Choline chloride-based DES combined with hydrogen-bond donors such as glycerol or ethylene glycol can extract rutin from *S. japonica* with efficiencies comparable to or better than methanol, while substantially reducing the use of toxic solvents [14–16]. Ultrasound-assisted DES extraction from other rutin-containing species, such as *Ilex asprella*, has been optimized using response surface methodology to maximize yield and minimize solvent volume [17].

Other innovative extraction techniques include microwave-assisted extraction, which improves mass transfer and reduces processing time; pressurized liquid extraction; and, to a more limited extent, supercritical CO_2-based methods with co-solvents for polar flavonoids [3]. These approaches not only improve yield and sustainability but also integrate well with downstream purification steps, enabling the production of highly enriched, standardized rutin extracts suitable for nutraceutical or pharmaceutical applications [3,14–17].

2.3 Analytical Characterization

Robust analytical methods are essential for quality control of rutin-containing herbal drugs and formulations.

2.3.1 HPLC and UHPLC

Reversed-phase high-performance liquid chromatography (RP-HPLC) is the primary tool for routine quantification of rutin in plant materials and finished products [3,18–21]. Typical methods use C18 columns with water–acetonitrile or water–methanol gradients, UV detection between 254 and 370 nm, and analysis times under 20 minutes [18,19]. Validated RP-HPLC assays have been reported for quantification of rutin in *Croton blanchetianus* herbal drugs and commercial products,[18] for simultaneous estimation of rutin and quercetin in *Morus alba* leaf extracts,[19] and for marker-based standardization of complex polyherbal preparations [21].

Ultra-high-performance liquid chromatography coupled with tandem mass spectrometry (UHPLC-MS/MS) further increases sensitivity and selectivity, enabling simultaneous measurement of multiple flavonoids, including rutin, in biological fluids, plant extracts, and functional foods [20]. Such methods are particularly valuable for pharmacokinetic and

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bioavailability studies because they can reliably quantify low plasma levels and phase-II metabolites [20].

2.3.2 LC–MS, NMR, and spectroscopic methods

LC–electrospray ionization mass spectrometry (LC-ESI-MS^n) and high-resolution LC–MS provide detailed fragmentation patterns and accurate mass measurements that confirm the identity of rutin in complex matrices and differentiate it from isomeric quercetin glycosides [18,20]. Nuclear magnetic resonance (^1H and ^{13}C NMR) spectroscopy is used to determine glycosidic linkages and sugar configurations, confirming the presence of rutinose at C-3[3]. UV–visible spectroscopy shows characteristic λ_{max} values around 257 and 355-360 nm, reflecting the flavonol chromophore; while not specific on its own, it is useful in combination with chromatographic profiles as part of fingerprinting and quality-control strategies [1,3,11].

2.3.3 Standardization and quantification in formulations

Validated chromatographic methods that address linearity, precision, accuracy, and robustness are now widely applied to:

- standardize crude herbal drugs (e.g., *S. japonica*, *Morus alba*, *Croton* spp., *Dimorphandra* spp.) [18,19,21];
- monitor rutin content in polyherbal formulations, nutraceutical supplements, and cosmetic preparations [3,18,21];
- evaluate rutin levels in functional foods, particularly buckwheat-based products and citrus-derived ingredients [5,10–12].

Together, these analytical advances support consistent manufacturing and enable meaningful correlation of dose, exposure, and pharmacodynamic effects in pre-clinical and clinical studies.

3. Pharmacological and Therapeutic Activities

3.1 Antioxidant and Anti-inflammatory Activity

Rutin is consistently reported as a potent antioxidant and anti-inflammatory agent *in vitro* and *in vivo* [1–3]. It directly scavenges reactive oxygen species (ROS) and reactive nitrogen species (RNS), chelates transition metals involved in Fenton chemistry, and up-regulates endogenous defense enzymes via activation of the Nrf2/ARE pathway [1–3]. At the same time, rutin inhibits NF-κB activation and down-regulates pro-inflammatory mediators such as COX-2, inducible nitric oxide synthase (iNOS), tumor necrosis factor-α, interleukin (IL)-1β, and IL-6 in diverse cell types [1–3].

These mechanisms translate into beneficial effects in models of hyperglycemia, metabolic syndrome, and tissue injury, where rutin reduces lipid peroxidation and restores superoxide dismutase, catalase, and glutathione peroxidase activities [1–3]. Topical and hydrogel formulations containing rutin have also shown anti-inflammatory activity in carrageenan-

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induced paw edema and concurrent antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*, indicating the feasibility of local delivery for inflammatory skin conditions [38].

Overall, pleiotropic redox and cytokine modulation underpins many of rutin's downstream protective actions in the cardiovascular, nervous, hepatic, and renal systems.

3.2 Cardioprotective and Antihypertensive Effects

Cardiovascular protection by rutin has been documented in multiple experimental models and in early clinical studies[1–3,22]. In myocardial ischemia–reperfusion injury, rutin reduces oxidative damage, preserves mitochondrial function, and activates pro-survival signaling pathways such as ERK1/2 and PI3K/Akt, thereby limiting infarct size and improving functional recovery [1,2]. Rutin improves endothelial function through enhanced nitric oxide bioavailability and reduced endothelin-1, contributing to vasorelaxation and lowered vascular resistance [1–3].

In diet-induced dyslipidemia models, rutin lowers total cholesterol, LDL-cholesterol, and triglycerides while increasing HDL-cholesterol, partly via modulation of PPARγ and suppression of hepatic lipogenesis [2,3]. Buckwheat-based diets, which provide naturally high rutin intake, have been associated with improved lipid profiles and reduced cardiovascular risk markers in animal and human studies [5,6,10].

Clinically, a double-blind, placebo-controlled trial in patients with type 2 diabetes mellitus showed that 1 g/day of rutin for 8 weeks significantly reduced systolic and diastolic blood pressure and improved antioxidant enzyme activities compared with placebo [22]. Earlier supplementation work in diabetes also suggested improvements in glycemic control and general health indices with rutin-containing regimens [23]. Collectively, these data support a cardioprotective and mild antihypertensive role of rutin; however, larger and longer-duration clinical trials are still required to define optimal dosing and long-term safety [2,22].

3.3 Neuroprotective and Cognitive Benefits

Neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and glioblastoma involve oxidative stress, neuroinflammation, mitochondrial dysfunction, and dysregulated cell death pathways. Rutin has emerged as a promising neuroprotective flavonoid [1,5].

A recent mechanistic review outlined how rutin exerts neuroprotection by attenuating oxidative stress and inflammation, inhibiting neuronal apoptosis, modulating neurotransmitter systems, and protecting the blood-brain barrier [5]. In Alzheimer's disease models, rutin reduces amyloid-β-induced oxidative damage and inflammatory cytokine production, improves synaptic plasticity markers, and enhances learning and memory in behavioral tests [1,5]. In Parkinsonian models, it mitigates dopaminergic neuron loss, decreases nigrostriatal oxidative damage, and improves motor performance [1,5].

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Rutin also exhibits analgesic, anticonvulsant, and antidepressant-like effects in neuropathic pain and mood disorder models, linked to modulation of monoaminergic and GABAergic pathways [1,5]. In glioblastoma models, rutin inhibits glioma cell proliferation, modulates microglial activation, and lowers pro-inflammatory mediators, suggesting potential as an adjuvant in neuro-oncology [31]. Nano-formulations and alternative delivery routes such as intranasal administration are being explored to overcome the limited blood–brain barrier permeability and modest systemic bioavailability of conventional oral rutin [3,5,29].

3.4 Anticancer Properties

Rutin displays anticancer activity across a range of malignancies, including breast, lung, colon, cervical, prostate cancer, and glioblastoma [1,2,29–31]. Mechanistically, it induces apoptosis via intrinsic (mitochondrial) and extrinsic pathways, causes cell-cycle arrest at G0/G1 or G2/M, inhibits angiogenesis and metastasis, and attenuates chronic inflammation and oxidative DNA damage [1,2,30].

Rutin modulates key signaling cascades such as PI3K/Akt/mTOR, MAPK (ERK, JNK, p38), NF-κB, and p53, leading to reduced cell proliferation and enhanced apoptosis [30]. In chemoresistant triple-negative breast cancer models, rutin reverses multidrug resistance by inhibiting efflux transporters such as P-glycoprotein and breast cancer resistance protein and can restore sensitivity to conventional chemotherapy [29,32,39]. Rutin-chitosan nanoconjugates, quercetin–rutin nano-formulations, and other nano-delivery systems often show greater cytotoxicity and tumor growth inhibition than free rutin in pre-clinical studies, demonstrating the value of formulation optimization [29,32].

Although clinical data specifically evaluating rutin as an anticancer drug are still lacking, pre-clinical evidence supports its use as a chemopreventive nutraceutical and potential adjuvant to chemotherapy, pending rigorous human trials [2,29,30].

3.5 Hepatoprotective and Nephroprotective Actions

3.5.1 Hepatoprotective effects

The liver is highly susceptible to oxidative and inflammatory injury induced by xenobiotics, high-fat diets, and metabolic disease. Rutin has demonstrated consistent hepatoprotective effects in a variety of experimental models [3,25,36]. In a mouse model of non-alcoholic fatty liver disease, rutin reduced hepatic triglyceride accumulation, improved lipid metabolism, and attenuated oxidative injury, partly via modulation of autophagy and inflammatory cytokines [25]. In classical hepatotoxicity models induced by carbon tetrachloride, paracetamol, and other toxins, rutin decreases lipid peroxidation, restores antioxidant enzyme activities, and suppresses stellate cell activation and fibrotic markers [1,3,36]. A contemporary review of rutin-associated hepatoprotection concluded that the compound

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consistently attenuates liver injury in both alcoholic and non-alcoholic liver disease models [36, 37].

3.5.2 Nephroprotective effects

Rutin also exerts kidney-protective effects in models of both acute and chronic renal injury [26–28]. In lipopolysaccharide-induced acute kidney injury, rutin lowers serum creatinine and blood urea nitrogen, improves renal histology, and normalizes renal expression of NF-κB, Toll-like receptor 4, COX-2, SIRT1, tumor necrosis factor-α, IL-6, and caspase-3, indicating combined anti-oxidative, anti-inflammatory, and anti-apoptotic actions [26].

It protects against vancomycin-induced nephrotoxicity by limiting oxidative stress, apoptosis, and inflammatory signaling, and nano-encapsulation further enhances these protective effects [27,29]. Rutin-loaded bilosomes designed to improve solubility and oral bioavailability significantly ameliorated potassium dichromate-induced acute kidney injury, improving renal function parameters and histological scores [28].

3.6 Antidiabetic and Anti-obesity Effects

Rutin influences glucose and lipid metabolism at multiple levels and has demonstrated antidiabetic and anti-obesity effects in pre-clinical and early clinical studies [1–3,22–24]. In streptozotocin-induced diabetic rats, rutin alone and in combination with metformin improve fasting blood glucose, insulin sensitivity, and lipid profiles, while enhancing vascular reactivity and endothelial function [24]. Supplementation studies in patients with type 2 diabetes mellitus have reported improvements in glycemic parameters, oxidative stress markers, and overall health indices when rutin is added to standard care [22,23].

Mechanistic work indicates that rutin may increase insulin secretion, enhance insulin signaling, inhibit intestinal α-amylase and glucose absorption, and modulate adipokines and inflammatory pathways relevant to insulin resistance [1–3]. In high-fat diet models, rutin and nano-rutin preparations reduce body-weight gain and adipose tissue mass, improve lipid profiles, and attenuate obesity-related oxidative stress and inflammation, thereby protecting against obesity-associated liver and kidney dysfunction [3,24,25]. Given the strong overlap between cardiometabolic disease, fatty liver disease, and chronic kidney disease, these integrated effects make rutin an attractive multi-target nutraceutical candidate.

3.7 Antimicrobial and Antiviral Activity

Rutin exhibits broad antimicrobial activity, though generally with modest potency compared with conventional antibiotics. Its more realistic role may be as an adjuvant or resistance-modifying agent [29,33,38].

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3.7.1 Antibacterial and antifungal actions

In vitro, rutin shows activity against Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, as well as against fungal pathogens such as *Candida albicans* [33,34,38]. Proposed mechanisms include disruption of cell membranes, interference with nucleic acid synthesis, and attenuation of quorum sensing [29,33]. Rutin can also modify antibiotic activity, lowering minimum inhibitory concentrations of β-lactams and aminoglycosides against certain resistant strains, likely by efflux pump inhibition or increased membrane permeability [33].

Recent work on photoactivated flavonoid complexes such as Rutin-Gal (III) has demonstrated enhanced antibacterial efficacy against multidrug-resistant *A. baumannii* under antimicrobial photodynamic therapy, opening an interesting niche for rutin-based adjuvants in difficult-to-treat infections [34].

3.7.2 Antiviral properties

Computational and experimental studies suggest that rutin may also exhibit antiviral activity. In silico screening and docking studies have identified rutin as a potential inhibitor of SARS-CoV-2 main protease and other viral targets, with favorable binding affinities and pharmacophore features [35]. Earlier data indicate activity against herpesviruses and influenza viruses, although in vitro potency is modest and clinical extrapolation is premature [1–3]. In addition, rutin's immunomodulatory and antioxidant actions may indirectly support host defense during viral infections.

Although rutin is unlikely to replace standard antimicrobials, these findings support further research into its role as an adjunct, particularly in topical formulations, oral care, and device-related infections, as well as in antiviral nutraceutical combinations.

4. Future Perspectives and Research Gaps

4.1 Emerging Areas: Precision Medicine and Nutraceutical Applications

Advances in genomics, metabolomics, and microbiome research offer opportunities to integrate rutin into precision nutrition and precision medicine strategies. Inter-individual variability in flavonoid metabolism driven by differences in gut microbiota composition, conjugating enzymes, and transporter expression can significantly influence response to rutin-rich diets or supplements [2–4]. Future studies should stratify participants by such factors and explore personalized dosing and formulation approaches.

In the nutraceutical arena, rutin is increasingly incorporated into functional foods (e.g., buckwheat-based products, fortified beverages), dietary supplements, and cosmeceuticals, often in combination with vitamin C or other polyphenols to exploit synergistic antioxidant and vasoprotective effects [2,3,5,7]. Regulatory frameworks will need to address

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standardization of content, quality-control specifications, and clinical substantiation of health claims.

4.2 Overcoming Biopharmaceutical Limitations

Poor aqueous solubility, limited membrane permeability, and extensive first-pass metabolism constrain the oral bioavailability of rutin. To address these issues, multiple formulation strategies are being evaluated [3,4,29]. Nano- and micro-carriers such as liposomes, solid lipid nanoparticles, polymeric nanoconjugates, bilosomes, and niosomes can improve solubility, protect against degradation, and enhance tissue targeting [28,29,37]. Bioconjugates and prodrugs for example, fatty-acid or sugar-modified rutin derivatives aim to modulate absorption and pharmacokinetics [4,29].

Alternative routes of administration, including sublingual, transdermal, and intranasal delivery, are being explored to bypass hepatic first-pass metabolism and increase systemic or central nervous system exposure [3,5,37]. While many of these approaches show promising pre-clinical results, few have advanced into clinical trials; direct comparisons among platforms, stability and safety profiling, and pharmacokinetic–pharmacodynamic modeling will be crucial for rational selection.

4.3 Need for Large-scale Clinical Validation

Despite compelling pre-clinical data, human evidence for many of rutin's purported benefits remains limited. Existing clinical studies are generally small, short-term, and often use combination products rather than purified rutin [2,22,23,36]. Large randomized, placebo-controlled trials are required to:

- define effective and safe dose ranges for cardiometabolic, neuroprotective, hepatoprotective, and nephroprotective indications;
- evaluate clinically meaningful endpoints (e.g. major cardiovascular events, cognitive decline, liver and renal outcomes) rather than surrogate markers alone;
- assess interactions with standard pharmacotherapies, especially antiplatelet agents, anticoagulants, antihypertensives, and hypoglycemics [2,22,36].

Safety in special populations, including pregnant women, the elderly, and patients with advanced hepatic or renal impairment, also warrants systematic evaluation.

4.4 Computational Approaches in Drug Design

Computational tools such as molecular docking, molecular dynamics simulations, pharmacophore modeling, network pharmacology, and in silico ADMET predictions are increasingly used to explore rutin's interaction landscape and guide derivative design [29,30,35]. Docking studies have highlighted the favorable binding of rutin to a variety of enzymes and receptors, including viral proteases and cancer-related kinases. At the same

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time, network pharmacology analyses map its multi-target effects across inflammatory, metabolic, and apoptotic pathways [29,30,35].

Such systems-level approaches can help prioritize targets, predict off-target interactions and drug–drug interactions, and rationally design rutin analogues or conjugates with improved potency, selectivity, and pharmacokinetic properties. Integrating computational predictions with high-quality experimental validation will be a key step in moving rutin from a broadly active nutraceutical to a template for targeted drug development.

5. Conclusion

Rutin is a structurally well-characterized flavonol glycoside with a broad spectrum of biological activities relevant to cardiovascular, neurodegenerative, metabolic, hepatic, renal, infectious, and neoplastic diseases. Advances in phytochemistry, green extraction, and analytical methods have enabled the reliable standardization of rutin-rich extracts from plants such as Sophora japonica and buckwheat, facilitating their use as nutraceuticals and potential adjuvant therapies.

Mechanistically, rutin acts as a powerful antioxidant and anti-inflammatory agent, modulating key signaling pathways (NF-κB, Nrf2, PI3K/Akt, MAPK, SIRT1, apoptotic cascades) and improving endothelial function, lipid and glucose metabolism, and cellular resilience to stress. Preclinical data consistently support cardioprotective, neuroprotective, hepatoprotective, nephroprotective, anticancer, and antimicrobial benefits. Early clinical studies in diabetes and vascular disorders add human-level support, particularly for blood pressure reduction and antioxidant effects, but remain small and heterogeneous.

Major challenges include low aqueous solubility, modest oral bioavailability, and the paucity of large, high-quality clinical trials. Emerging nano-formulations, prodrugs, and alternative delivery routes offer promising solutions, while computational approaches can accelerate the design of improved rutin analogs and formulations.

In summary, rutin represents a prototypical multi-target phytochemical with substantial translational potential. Realizing this potential will require rigorous clinical validation, thoughtful integration into evidence-based nutritional and therapeutic strategies, and careful attention to standardization and safety.

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